COVID-19 case fatality and Parkinson's disease

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Key Words: Parkinson's disease, Coronavirus disease 2019 (COVID-19), Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), Case fatality

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Main text

Case fatality rates (CFR) of the novel 2019 coronavirus disease (COVID-19) have been reported ranging from 0% to 40% among Parkinson's disease (PD) patients. However, because of small sample sizes and the lack of large matched comparison groups[1-4], previous studies have not clarified whether PD is an independent risk factor for death. The goal of our study was to determine whether PD patients had a higher COVID-19 CFR.

We compared COVID-19 CFR in PD patients with a large, demographically matched population via the TriNetX COVID-19 research network, a health research database with deidentified

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/mds.28325

medical records of over 50 million patients mostly from the USA. As of July 15, 2020, this database listed 79,049 adult COVID-19 patients, 694 of whom had PD. On September 9, 2020, we extracted mortality data for this cohort. We included this eight-week delay to allow identified cases to resolve. Among 78,355 COVID-19 patients without PD, 4,290 died compared to 148 of the 694 patients with PD (5.5% Non-PD vs. 21.3% PD, $p<0.001$, $\chi 2$ test).

The non-PD and PD groups had different age distribution (median age 50 vs. 79), sex balance (female 55.3% vs. 39.8 %), and racial composition (African American 19.7% vs 9.7%). Additionally, CFRs from COVID-19 have been reported as higher in males vs. females[5], African Americans vs. Caucasians[6], and elderly vs. younger patients[5].

We accounted for these differences using logistic regression with age, sex, and race as covariates. This analysis revealed that the risk of dying from COVID-19 was significantly elevated in the PD group (odds ratio (OR): 1.27, 95% confidence interval (CI): 1.04-1.53, p=0.016; Fig 1A-B).

To assess residual confounders, we matched five COVID-19 patients without PD to each PD patient with the exact age, sex, and race. We then performed a conditional logistic regression and found that PD patients had a significantly higher risk of dying from COVID-19 compared to patients without PD (OR = 1.30, 95% CI: 1.13-1.49, $p<0.001$). We further replicated the analysis with 1,000 random matchings, and found similar results, with the effect being statistically significant in all but 2 replications.

In summary, we leveraged the TriNetX database and found that COVID-19-related CFR was increased in PD patients, independent of age, sex, and race. These results are not without limitations. First, the TriNetX COVID-19 research network includes over 40 healthcare

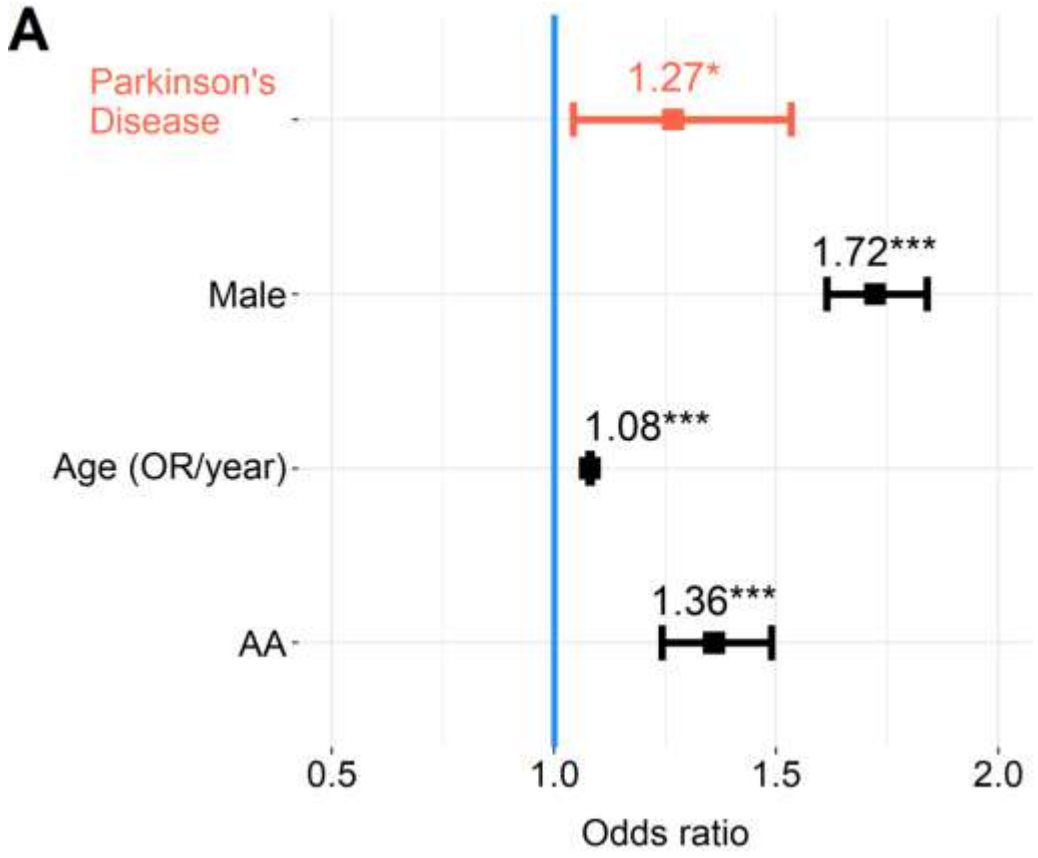
organizations primarily in the USA. We were unable to account for confounding regional factors that could increase mortality. Additionally, this database lacks information on key comorbidities. Second, CFRs from COVID-19 have decreased with increased access to testing. It will be important to conduct follow-up studies. Third, this study only reports an association between COVID-19-related mortality and a diagnosis of PD; however, in this context designs better suited to causal inference are challenging. Finally, the TriNetX database does not include information on recovery. Despite these limitations, our results indicate that it will be critical to develop effective strategies whereby healthcare providers can prevent the transmission of COVID-19 while providing neurological care to patients with PD.

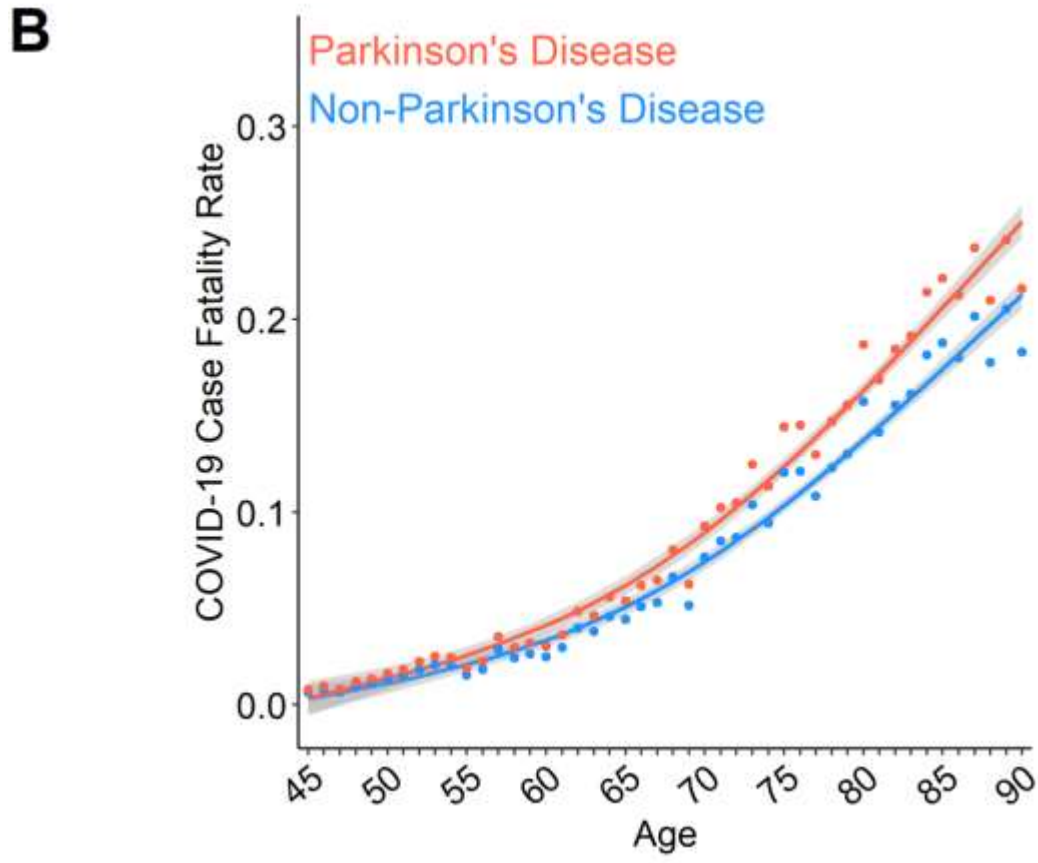
Author contributions:

QZ and NN conceived and designed the study, JES, JLS, KN and QZ performed data analysis, QZ, JLS, GA, JES and NN wrote the manuscript.

Figure legends:

Figure 1: COVID-19 patients with PD have an increased case fatality rate (CFR). A) COVID-19 patients with PD (n=694) have an increased CFR compared to those without PD (n=78,355, odds ratio: 1.27, 95% confidence interval: 1.04-1.53, p=0.016). Logistic regression was performed with age, sex, and race included as covariates. Data from 79,049 COVID-19 patients in the TriNetX COVID-19 research network. Each dot represents the model fit of each year for PD patients and those without PD. B) COVID-19 CFR was higher across age groups >50 years.





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